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Lipid Peroxidation, Oxidative Stress and Its Correlation with Glycated Hb in Type2 Diabetes Of North West Punjabi Population

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ABSTRACT

Background: In India, type 2 diabetes mellitus(DM) is an epidemic disorder because of social impact and changes in way of life. According to the WHO, 72 million people were affected by DM in India in the year 2017, a figure expected to almost double to 134 million by 2025, the largest number in any country in the world. **Aims and Objectives**: The aim is to investigate the Lipid Peroxidation, Oxidative stress and its correlation with Glycated Hb in Type2 Diabetes of North West Punjabi population. **Material and Methods**: This cross- sectional study included 200 subjects, 100 were type 2 diabetic patients and 100 were healthy non-diabetic individuals. The data were analyzed using a t test. **Results**; The results showed positive correlation between HbA1c and fasting blood Glucose (r = 0.417, p= 0.000) with MDA(r=0.340,p=0.000), Triglycerides (r = 0.214, p= 0.003), Total cholesterol(r= 0.306,p=<0.002), Non HDL(r=0.322,p=0.001), LDL(r=0.327,p=0.001), VLDL(r=0.318,p=<0.001), with glycated Hb in patients of type 2 diabetes mellitus. Similarly, with HbA1c and with BMI (r= 0.422,p=0.000) with glycated Hb in patients of type 2 diabetes mellitus, Whereas negative correlation was observed between HbA1c and other parameters like HDL (r=0.197, p=0.050), HDL to LDL ratio(r= 0.144,p= 0.152), SOD(r=0.025,p=0.803). **Conclusion**; As glycemic control of diabetic patient decreases, this increase of glycated Hb leads to atherogenic lipid profile along with increased lipid peroxidation, thus making the individual susceptible to various complications, both macrovascular and microvascular.

Key Words: *glycated hemoglobin, lipid profile, dyslipidemia, malondialdehyde, superoxide dismutase*

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INTRODUCTION

Globally, type 2 diabetes mellitus (T2DM) is a swiftly escalating public health issue with noteworthy effects on human health, living standards, the economy and health care systems[1].Statistics from the International Diabetes Federation (IDF) indicate that 425 million adults worldwide have diabetes mellitus (DM) and that by 2045, the number of DM patients will be 629 million and 352 million people will be at risk of developing T2DM[2].

Hyperglycemia activates certain upstream events that lead to mitochondrial overproduction of reactive oxygen species, which increases the oxidative stress status[3,4]. Oxidative stress mediates insulin resistance and hence accelerates the progression of glucose intolerance to diabetes mellitus and its various complications[5].

T2DM patients are prone to diabetic dyslipidemia, which puts them at risk of developing macrovascular (stroke, peripheral vascular disease and coronary artery disease [CAD]) and microvascular (nephropathy, neuropathy and retinopathy) diseases[6]. Naqvi et al (2017) have reported that, for T2DM patients, one of the most common complications linked with uncontrolled hyperglycemia is dyslipidemia[7].

Glycated hemoglobin (HbA1c) levels are routinely measured in diabetics to monitor their glycemic control. The goal is to achieve a level below 7%. Levels of HbA1c can be affected by multiple factors, including sugar intake, exercise and adherence to medications. Some studies have reported that HbA1c could potentially be utilized as a possible biomarker for predicting dyslipidemia and cardiovascular disease (CVD)[8.9].

The level of circulating HbA1c is taken as the gold standard of glycemic control, and regulating it is imperative for avoiding T2DM complications. HbA1c values not only reflect glycemic control but are also the main factor in determining the risk of diabetes-related complications.[10] and mortality[11].

There are several conflicting results in the literature, such as a Turkish study that found a significant relationship between total cholesterol (TC), LDL, triglycerides (TGs) and HbA1c,[12] while others reported no considerable relationship[13]. Similarly, while one study reported a significant negative relationship between HbA1c and LDLC[14]. Others reported the opposite results[9]. Importantly, a recent study revealed a positive relationship between HbA1c and high TGs, concluding that HbA1c could be a sign of TG levels and thatit may predict CVD risk factors in T2DM[7].

It has been shown that non-HDL-C is a strong predictor for future cardiovascular risk in patients with or without exhibiting symptoms of vascular diseases. Furthermore, it has been suggested as a secondary therapeutic target following LDL-C among patients with raised Triglyceride (TG) by the National Cholesterol Education Program Adult Treatment Panel III [15] owing to its proatherogenic, apo-B-containing lipoprotein fraction of circulating lipid [16].Type 2 diabetic patients have significantly elevated levels of non-HDL-C compared to controls; therefore, it can be used as a dyslipidemia marker and a predictorfor CVD [17,18] and vascular inflammation [19] in type 2 diabetic patients.

Malondialdehyde (MDA), a toxic stable aldehyde, is produced by the peroxidation of lipids by the reactive oxygen species [20]. Several protective mechanisms are in place to prevent the histological damage it causes. One is an antioxidant enzyme, superoxide dismutase (SOD), which catalyzes the dismutation of one of the reactive oxygen species, superoxide radical, into oxygen and water [21]. Both MDA and SOD can be used as biological markers to quantify oxidative stress status [22]. Overweight and obesity have long been regarded as health risks associated with the type 2 diabetes [23].

Our study investigated the Lipid Peroxidation, Oxidative stress and its correlation with Glycated Hb in Type2 Diabetes of North West Punjabi population.

MATERIAL AND METHODS;

This cross-sectional study was carried out in the Department of Biochemistry, Government Medical College & Guru Nanak Dev Hospital Amritsar, Punjab, from January 2022 to March 2023. Of the 200 subjects, 100 were type 2 diabetic patients and 100 were healthy non- diabetic individuals. Healthy non diabetic individuals serve as controls for this study and were selected from the general population who visited the hospital's outpatient department. The research was authorized by the Institutional Ethics Committee. All participants provided informed consent. They were exposed to a complete history and examination, as well as biochemical and special tests.

Inclusion criteria

Diabetics: Patients with type II diabetics mellitus confirmed by fasting blood sugar, under medication (hypoglycemic drugs and insulin) in the age group of 26-70 years.
Controls: Normal healthy non diabetic individuals in age group of 26-70 years.

Exclusion criteria

The subjects with liver disease, renal disease, thyroid disease, tuberculosis, hypertension, pancreatitis, Coronary artery disease (CAD, previous history) Stroke, individuals on drugs like gluco-corticoids, Nicotinic acid, Thyroid hormones, β adrenergic antagonists and thiazidediuretics, drug addicts patient with endocrinopathies such as acromegaly, patients with down syndrome were excluded from the present study.

Sample collection and storage

Under aseptic conditions, 5 ml of venous fasting blood was collected. Out of this 1ml was collected in EDTA for estimation of HbA1C and 1 ml collected in sodium fluoride vial for estimation of plasma glucose. 3 ml of Blood was Centrifuged the sample at 3000rpm for 5min to obtain serum for estimation of various parameters ie. MDA, SOD and lipid profile.

Biochemical measurement :

1. Fasting blood glucose by GOD-POD methods [24].
2. Glycated HbA1c by ion exchange methods [25].
3. Total cholesterol(TC) by enzymatic endpoint CHOD-POD methods [24].
4. Triglycerides (TG) by enzymatic glycerol phosphate oxidase/peroxidase method [24].
5. High-density lipoprotein cholesterol (HDL-c) by Peg precipitation method [24].
6. Low-density lipoprotein cholesterol (LDL-c) by Friedewald's Formula [24].
7. Very low-density lipoprotein cholesterol (VLDL-c) by Friedewald's equation LDL-c = Tc-HdL-c (TG/5)
8. Non HDL = Total cholesterol – HDL-c
9. HDL /LDL = HDL to LDL ratio
10. Malondialdehyde (MDA) by kei Satoh [26].
11. Superoxide dismutase (SOD) by Marklund [27].
12. Body Mass Index (BMI) = weight in kg divided by height in meters squared.

Statistical analysis

The data thus generated was analyzed Statistically using student 't' test to compare the mean of two groups. ANOVA for comparison of mean in more than two groups. Pearson's coefficient of correlation was used to calculate the correlation between different parameters. p
<0.05 was considered statistically significant.

RESULTS

Out of 100 type 2 diabetes participants, 52 were men and 48 were women. Similar to the study group, the control group had 100 non-diabetic participants, 58 men and 42 women. 17

% diabetics and 43 % non-diabetics were sharing the age group <= 40. 57 % diabetics and 41

% non-diabetics were sharing the age group of 41-60, the maximum number of diabetics. On the other hand, age group shared >60, 26 % were diabetics, and 16 % were non-diabetics. Diabetics have a age of 51.33 ± 11.2, while non-diabetics had a Mean age of 44.9 ± 14.4 years.

The HbA1c levels of diabetics were divided into four groups based on their glycated hemoglobin levels in the present study: Group I (=5.4%) had a mean value of 4.29±1.23; Group II (>5.4%-6.4%) had a mean value of 6.06±0.23; Group III (>6.4%-8.0%) had a mean value of 7.29±0.48; and Group IV (>8.0%) had a mean value of 10.62±1.84, which was statistically highly significant (p=0.00).

Table-1: Segregation of Patients According to levels of glycated (Hb)

S.NO	GROUP	MEAN±SD
		HbA1C %
I	Control	4.11±1.12
II	Group 1 patient<=5.4%	4.29±1.23
III	Group 2 patient >5.4% -6.4%	6.06±0.23**
IV	Group 3 patient >6.4% - 8.0%	7.29±0.48***,*
V	Group 4 patient >8.0	10.62±1.84***,***,***

When the Diabetics were divided according to glycated Hb, which was statistically highly significant. (p=0.00). Group I was compared to groups II (p= **0.11 not significant), III (p= ***0.00 highly significant), and IV (p= ***0.00 highly significant). Group II was compared to Group III (p=*0.03 significant), IV (p=***0.00 highly significant). When Group III and Group IV werecompared, p=***0.00 was found to be highly significant.

Table-2: Mean Value of FBS in Diabetic Patients According to HbA1C

S.NO	GROUP	MEAN±SD
		FBS (mg%)
I	Control	87.59±7.13
II	Group 1 patient<=5.4%	133.36±31.56
III	Group 2 patient >5.4% -6.4%	139.90±31.56**
IV	Group 3 patient >6.4% - 8.0%	238.14±247.98**,*
V	Group 4 patient >8.0	252.11±62.26**,***,**

When the Diabetics were divided according to glycated Hb, it was observed that the level of Fasting blood Glucose increased as the glycated Hb levels increased, which was statistically significant. (p <0.05).

Group I was compared to groups II (p=**1.00 not significant), III (p=**0.48 not significant), and IV (p=**0.31 not significant). Group II was compared to Group III (p=*0.04significant), IV (p=***0.00 highly significant). When Group III and Group IV were compared, p=**0.97 was found to be not significant.

Table-3: Mean Value of Total Cholesterol and Triglycerides in Diabetic PatientsAccording to HbA1C

S.NO	GROUP	MEAN±SD	
		TOTAL CHOLESTEROL (mg%)	TRIGLYCERIDES (mg%)
I	Control	151.22±40.72	130.07±60.51
II	Group 1 patient <=5.4%	160.07±48.21	142.01±72.41
III	Group 2 patient >5.4%-6.4%	162.10±40.80**	159.40±65.09**
IV	Group 3 patient >6.4% - 8.0%	178.18±46.46**,**	232.65±97.81***,**
V	Group 4 patient >8.0	185.52±61.52**,**,**	235.20±167.30*,**,***

Total Cholesterol (p value **1.00, **0.92, **0.80, **0.78, **0.37, **0.95) **Not SignificantTriglycerides (p value **0.99, ***0.01, *0.04, **0.60, **0.59, ***1.00) *Significant, **Not Significant, ***Highly Significant.

When the Diabetics were divided according to glycated Hb, it was observed that levels of Total Cholesterol and Triglycerides both increased as the glycated Hb levels increased. The total cholesterol was not statistically significant (p> 0.05), but triglycerides were statistically Significant (p <0.05).

When Group I was compared with Group II, III and IV. Group II was compared with III and IV. When Group III was compared with group IV.

Table-4: Mean Value of Lipo Protein in Diabetic Patients According to HbA1C

S.NO	GROUP	MEAN±SD		
		HDL (mg%)	LDL (mg%)	VLDL (mg%)
I	Control	54.23±17.32	65.43±21.79	25.57±11.21
II	Group 1 patient <=5.4%	48.25±14.05	79.67±42.30	28.28±14.31
III	Group 2 patient >5.4% - 6.4%	46.23±7.554**	88.65±42.74**	31.85±13.02**
IV	Group 3 patient >6.4% - 8.0%	43.31±7.748**,**	92.98±54.16**,**	46.48±19.54**,**
V	Group 4 patient >8.0	40.05±7.891**,**,**	100.14±43.03**,**,**	57.59±58.92*,**,**

HDL (p value **0.96, **0.66, **0.24, **0.46, **0.22, **2.00) **Not SignificantLDL (p value **0.98, **0.95, **0.98, **0.94, **0.88, **0.94) **Not Significant
VLDL (p value **0.99, **0.14, *0.02, **0.81, **0.45, **0.51) *Significant, **Not Significant

When the Diabetics were divided according to glycated Hb, it was observed that levels of HDL decreased and LDL and VLDL both increased as the glycated Hb levels increased. Change in the levels, HDL and VLDL were statistically significant (p < 0.05), but LDL was not significant (p >0.05).

When Group I was compared with Group II, III and IV. Group II was compared with III and IV. When Group III was compared with group IV.

Table-5: Mean Value of HDL to LDL ratio and Non HDL in Diabetic Patients Accordingto HbA1C

S.NO	GROUP	MEAN±SD	
		HDL to LDL RATIO (mg%)	NON HDL (mg%)
I	Control	0.822±0.612	110.22± 31.23
II	Group 1 patient <=5.4%	0.722±0.556	111.72±34.04
III	Group 2 patient >5.4% - 6.4%	0.695±0.285**	123.63±39.21**
IV	Group 3 patient >6.4% - 8.0%	0.640±0.439**,**	134.87±46.26**,**
V	Group 4 patient >8.0	0.527±0.321**,**,**	139.29±58.81**,**,**

HDL to LDL ratio (p value **1.00, **0.99, **0.92, **0.90, **0.44, **0.88) **Not Significant
Non HDL (p value **0.97, **0.84, **0.74, **0.90, **0.67, **0.98) **Not Significant

When the Diabetics were divided according to glycated Hb, it was observed that levels of HDL to LDL ratio decreased and Non HDL increased as the glycated Hb levels increased. HDL to LDL ratio and Non HDL were statistically not significant (p >0.05).

When Group I was compared with Group II, III and IV. Group II was compared with III and IV. When Group III was compared with group IV.

Table-6: Mean Value of Antioxidant status in Diabetic Patients According to HbA1C

S.NO	GROUP	MEAN±SD	
		MDA (µmol/ml)	SOD (ml)
I	Control	2.5±1.58	1.12±0.416
II	Group 1 patient <=5.4%	6.55±1.41	0.832±0.331
III	Group 2 patient >5.4% - 6.4%	11.11±6.21**	0.802±0.279**
IV	Group 3 patient >6.4% - 8.0%	15.39±13.64**,**	0.752±0.245**,**
V	Group 4 patient >8.0	19.88±16.39**,**,**	0.722±0.196**,**,**

MDA (p value **0.44, **0.54, **0.11, **0.44, ***0.00, **0.54) **Not Significant, ***Highly Significant.
SOD (p value **0.99, **0.92, **0.84, **0.86, **0.72, **0.96) **Not Significant

When the Diabetics were divided according to glycated Hb, it was observed that levels of Lipid Peroxidation increased and SOD decreased as the glycated Hb levels increased. MDA was statistically significant. (p <0.05) and SOD were not statistically significant (p>0.05).

When Group I was compared with Group II, III and IV. Group II was compared with III and IV. When Group III was compared with Group IV.

Table-7: Mean Value of BMI in Diabetics Patients According to HbA1C

S.NO	GROUP	MEAN±SD
		BMI
I	Control	18.82±1.21
II	Group 1 patient <=5.4%	25.98±3.84
III	Group 2 patient >5.4% - 6.4%	26.04±3.22**
IV	Group 3 patient >6.4% - 8.0%	26.08±3.84**,**
V	Group 4 patient >8.0	26.22±4.48**,**,**

P value (**1.00, **1.00, **0.99, **1.00, **1.00, **1.00) **Not Significant.

When diabetics were separated according to glycated Hb levels, it was found that the level of BMI increased as the glycated Hb levels increased, which was statistically significant. (p<0.05). When Group I was compared with Group II, III and IV. Group II was compared with III and IV. When Group III was compared with Group IV.

Linear regression analysis showed positive correlation between HbA1c and fasting blood Glucose (r = 0.417, p= 0.000) (fig.1) with MDA(r=0.340,p=0.000), triglycerides (r = 0.214, p= 0.003) (fig.2), Total cholesterol(r= 0.306, p=<0.002), Non HDL(r=0.322,p=0.001), LDL(r= 0.327, p= 0.001), VLDL(r= 0.318,p=<0.001), with glycated HB in patients of type 2 diabetes mellitus. Similarly, with HbA1c and with BMI (r= 0.422,p=0.000) with glycated Hb in patients of type 2 diabetes mellitus, Whereas negative correlation was observed between HbA1c and other parameters like HDL (r= 0.197, p= 0.050), HDL to LDL ratio(r= 0.144,p= 0.152), SOD(r= 0.025,p=0.803).

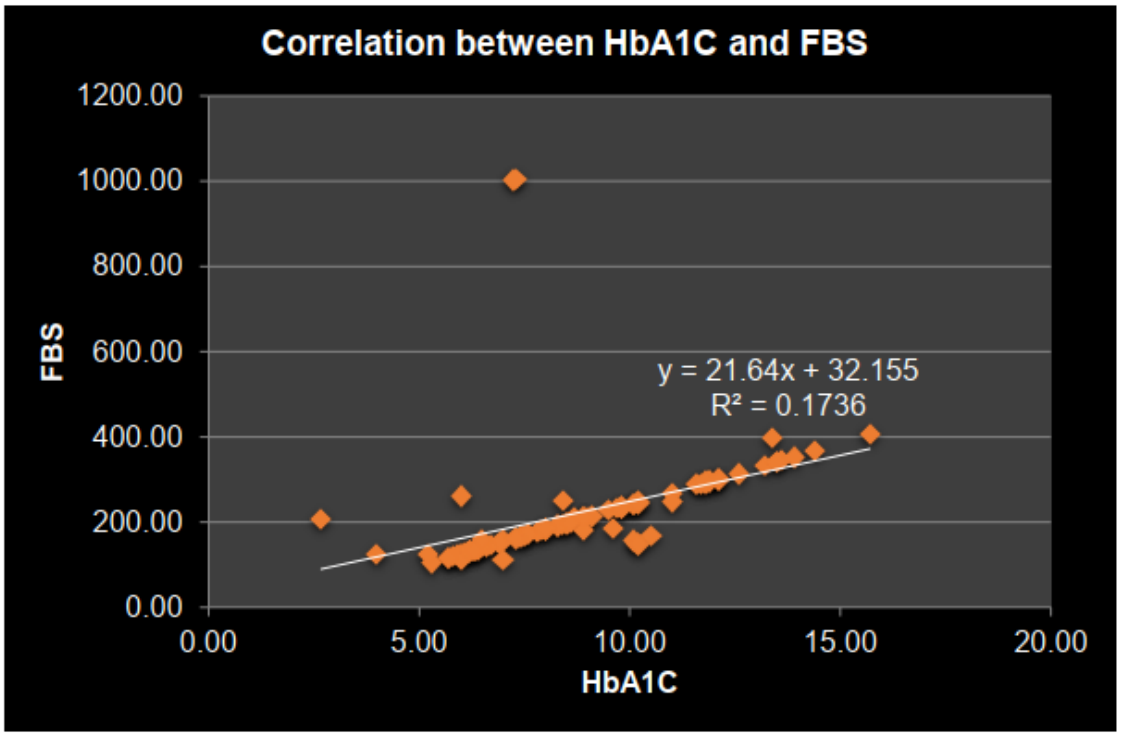

Figure-1: Correlation between HbA1c and FBS in diabetic patients

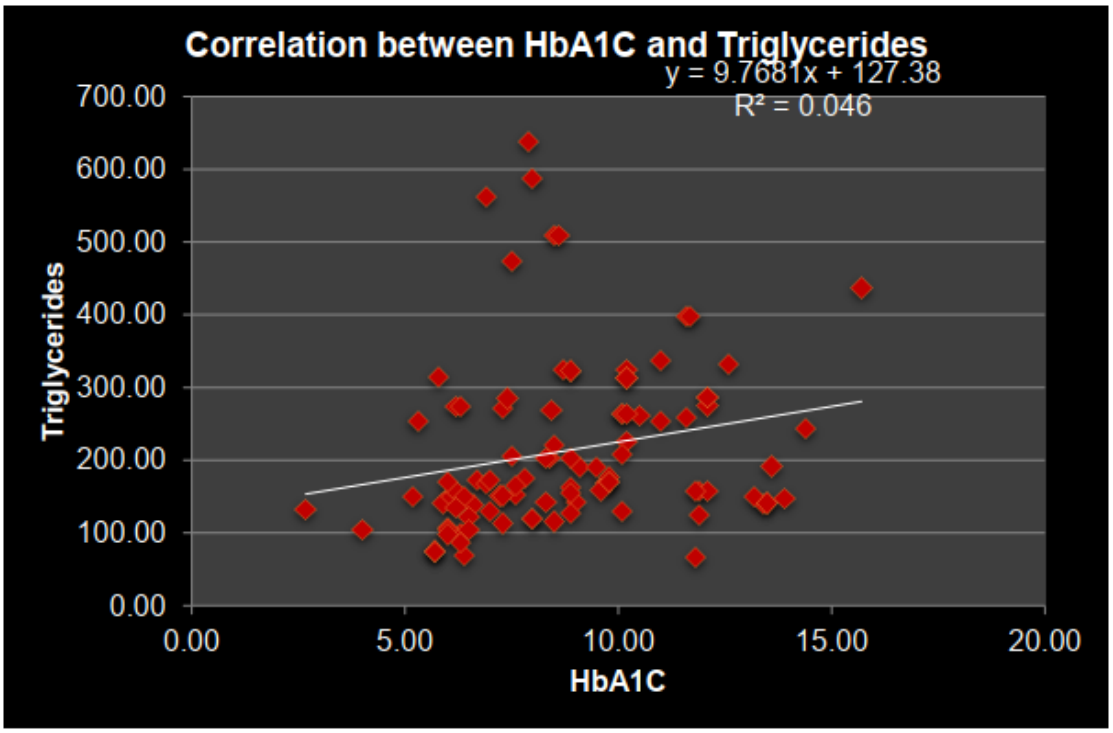

Figure-2: Correlation between HbA1c and Triglycerides in diabetic patients

DISSCUSSION;

DM is a complex and multifactorial disease. The metabolic dysregulation associated with diabetes causes secondary pathophysiologic changes in multiple organ systems that impose a heavy burden of morbidity and mortality from macrovascular and microvascular complications [28].

HbA1c levels could be employed as a possible biomarker for recognizing T2DM patients at risk of CVD and could be used as a guide for treating patients [7,29]. Our results display a significant positive relationship between HbA1c and TG. A similar correlation has been reported by several other studies [1,12] that found a positive relationship between HbA1c andhigh TG levels, in agreement with the present study, although one other study reported no correlation between HbA1c and TG [13].

The findings of this study and the others mentioned above indicates that HbA1c is a direct indicator of increased TG and indirectly helps in assessing the risk for macro- and microvascular problems [1,7].

In T2DM subjects, insulin resistance is considered as the cause of dyslipidemia. The reasons for increased TG levels in T2DM patients is an inadequate secretion or function of insulin that causes enhanced hepatic secretion of very low density lipoprotein (VLDL) along with thelate removal of TG-rich lipoproteins, mainly due to enhanced substrate levels for TG synthesis [30].

The present study found relationship between HbA1c and TC or LDL-C. Our results are consistent with the results of numerous other studies that have stated a significant relationshipbetween HbA1c and TC and LDL-C [1,6,29].

Further, our results show a statistically non-significant negative link between HbA1c and HDL-C. This is in agreement with the results from a few other studies [1,12]. but is inconsistent with several studies that reported a notable negative relationship between HbA1c and HDL-C [13,14,29]. Few other studies have described a positive relationship between HbA1c and HDL-C [9,31].

The linear regression analysis revealed the link between HbA1c values and TGs (p=0.020) and further showed that the correlation is independent of age, BMI, TC, LDL-C, HDL-C and FPG levels. Hussain et al (2017) also reported that HbA1c could be a predictor of TG, TC and LDL-C [1].

Thus the results of our study clearly indicate that there is strong association between the levels of HbA1c and HDL: LDL ratio. The levels of the Hb1Ac were found significantly higher in the diabetic group. Similarly the ratio of HDL: LDL was also altered due to the low levels of the protective high density lipoproteins. The results are similar to the previous studies done by Seema single and Indumati V, though they have taken LDL:HDL as the parameter because in their study the ratio was increased [32,33].

It has been reported that in Diabetic patients had a significant higher HbA1c (p= 0.00) levels and lower SOD (p= 0.00) levels when compared to control subjects. Significant positive correlation (r= 0.60, p= 0.00) and negative correlation (r= - 0.57, p= 0.001) was obtained between duration of diabetes and HbA1c, SOD levels respectively in diabetics. Also a significant negative correlation (r= - 0.75, p= 0.00) was observed between HbA1c and SOD levels in diabetic patients. In diabetics with poor glycemic control, SOD levels were significantly (p= 0.002) lower when compared to patients with good glycemic control[34].

According to another study, production of the oxygen free radicals was directly related to hyperglycaemia and the duration of diabetes. The MDA levels acted as a marker for lipid peroxidation i.e. oxidative stress and it was significantly increased in the cases as compared to the controls (P<0.001). In a state of poor metabolic control, increased serum MDA levels are expected. A positive correlation was found between the mean serum MDA levels and the mean HbA1c levels in the diabetic patients [35].

The mean ± SD of BMI in controls and type 2 diabetic subjects were in the range of group 1 patient (25.98±3.84), group 2 patient (26.04±3.22), and group 3 patient (26.08±3.84), group 4 patient(26.22±4.48) mg/dl and control group 18.82±1.21mg/dL, respectively. The mean value of BMI was higher in type 2 diabetic subjects compared to controls (Table-7). Various other studies done in our country demonstrated BMI among diabetic respectively; mean BMI was 24.85kg/m2 in Ramesh Chandra Thanna[36] and mean BMI was 23.95 ± 3.15 kg/m2 in a study done by L. S. Patil et al [37].

In the present study we also found positive correlation existed between BMI and HbA1c in type 2 a diabetic subject which was statistically significant. This is in accordance with Shetty J.K et al [38]. & Kim N.H et al [39].

CONCLUSION:

As glycemic control of diabetic patient decreases, this increase of glycated Hb leads to atherogenic lipid profile along with increased lipid peroxidation, thus making the individual susceptible to various complications, both macrovascular and microvascular.

REFERENCE

1. Hussain A, Ali I, Ijaz M, et al. Correlation between hemoglobin A1c and serum lipid profile in Afghani patients with type 2 diabetes: hemoglobin A1c prognosticates dyslipidemia. Ther Adv Endocrinol Metab. 2017;8:51–57. doi:10.1177/2042018817692296
2. International Diabetes Federation. IDF Diabetes Atlas. 8th ed; 2017. Available from: http://www.diabetesatlas.org/. Accessed August 8, 2019.
3. Brownlee M. The pathobiology of diabetic complications: a unifying mechanism. Diabetes. 2005;54(6):1615–1625. doi:10.2337/diabetes. 54.6.1615.
4. Gomes EC, Silva AN, de Oliveira MR. Oxidants, antioxidants, and the beneficial roles of exercise-induced

production of reactive species. Oxid Med Cell Longev. 2012;2012:756132. doi:10.1155/2012/ 756132.
5. Negre-Salvayre A, Salvayre R, Auge N, Pamplona R, Portero-Otın M. Hyperglycemia and glycation in diabetic complications. Antioxid Redox Signal. 2009;11(12):3071–3109. doi:10.1089/ars.2009.2484.
6. Kundu D, Saikia M, Paul T. Study of the correlation between total lipid profile and glycosylated hemoglobin among the indigenous population of Guwahati. Int J Life Sci Scienti Res. 2017;3:1175–1180.
7. Naqvi S, Naveed S, Ali Z, et al. Correlation between glycated hemoglobin and triglyceride level in type 2 diabetes mellitus. Cureus. 2017;9:e1347
8. Baranwal JK, Maskey R, Majhi S, et al. Association between level of HbA1c and lipid profile in T2DM patients attending diabetic OPD at BPKIHS. Health Renaiss. 2017;13:16– 23.
9. Naeem M, Khattak RM, Ur Rehman M, et al. The role of glycated hemoglobin (HbA1c) and serum lipid profile measurements to detect cardiovascular diseases in type 2 diabetic patients. South East Asia J Pub Health. 2016;5:30–34.
10. Stettler C, Allemann S, Juni P, et al. Glycemic control and macrovascular disease in types 1 and 2 diabetes mellitus: meta-analysis of randomized trials. Am Heart J. 2006;152:27–38.
11. Kranenburg G, van der Graaf Y, van der Leeuw J, et al. The relation between HbA1c and cardiovascular events in patients with type 2 diabetes with and without vascular disease. Diabet Care. 2015;38:1930–1936
12. Ozder A. Lipid profile abnormalities seen in T2DM patients in primary healthcare in Turkey: a cross-sectional study. Lipids Health Dis. 2014;13:183.
13. Sarkar S, Meshram A. HbA1c and lipid profile levels in the known type 2 diabetic group in the rural region of Vidarbha, Maharashtra, India. J Evid Based Med Health. 2017;4:1915– 1920. doi:10.18410/ jebmh/2017/374
14. Samdani TS, Mitra P, Rahim MA. Relationship of glycated haemoglobin with lipid profile among patients with type 2 diabetes mellitus. BIRDEM Med J. 2017;7:43–47. doi:10.3329/birdem.v7i1.31271
15. Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults. Executive summary of the third report of the national cholesterol education program (NCEP) expert panel on detection, evaluation, and treatment of high blood cholesterol in adults (Adult treatment panel III). JAMA 2001; 285:2486-97.
16. Mark L, Vallejo-Vaz AJ, Reiber I, Paragh G, Kondapally Seshasai SR, Ray KK, et al. Non-HDL cholesterol goal attainment and its relationship with triglyceride concentrations among diabetic subjects with cardiovascular disease: A nationwide survey of 2674 individuals in Hungary. Atherosclerosis 2015; 241:62-8.
17. Lu W, Resnick HE, Jablonski KA, Jones KL, Jain AK, Howard WJ, et al. Non-HDL cholesterol as a predictor of cardiovascular disease in type 2 diabetes: The strong heart study. Diabetes Care 2003; 26:16-23.
18. Pandeya A, Sharma M, Regmi P, Basukala A, Lamsal M. Pattern of dyslipidemia and evaluation of non-HDL cholesterol as a marker of risk factor for cardiovascular disease intype 2 diabetes mellitus. Nepal Med Coll J 2012; 14:278-82.
19. Wang CY, Chang TC. Non-HDL cholesterol level is reliable to be an early predictor for vascular inflammation in type 2 diabetes mellitus. J Clin Endocrinol Metab 2004; 89:4762-7.
20. Halliwell B, Chirico S. Lipid peroxidation: its mechanism, measurement, and significance. Am J Clin Nutr. 1993;57(5 Suppl): 715S–724S. doi:10.1093/ajcn/57.5.715S.
21. Davari S, Talaei SA, Alaei H, Salami M. Probiotics treatment improves diabetes-induced impairment of synaptic activity and cognitive function: behavioral and electrophysiological proofs for microbiome-gut-brain axis. Neuroscience. 2013;240:287–296. doi:10.1016/j. neuroscience.2013.02.055.
22. Ho E, Karimi Galougahi K, Liu CC, Bhindi R, Figtree GA. Biological markers of oxidative stress: applications to cardiovascular research and practice. Redox Biol. 2013;1(1):483–491. doi:10.1016/j. redox.2013.07.006.
23. Yach D, Stuckler D, Brownell KD. Epidemiologic and economic consequences of the global epidemics of obesity and diabetes. Nat Med. 2006;12(1):62–6.
24. Trinder P. for the determination of Glucose in Serum/ plasma and CSF. Clin Biochem 1969;6:24.https://www.scirp.org/(S(i43dyn45teexjx455qlt3d2q))/reference/ReferencesPapers.aspx?ReferenceID=130311
25. Nathan, D.M, et al. The clinical information value of the Glycosylated assay, The new England journal of medicine 1984; 341:46. https://pubmed.ncbi.nlm.nih.gov/6690962/
26. Satoh, K.(1978). Serum lipid peroxide in cerebrovascular disorders determined by a new colorimetric method. Clinica. Chemica. Acta. 37-43. doi: 10.1016/0009-8981(78)90081-5.
27. Marklund, S. and Marklund, G. (1974) Involvement of the Superoxide Anion Radical in the Autoxidation of Pyrogallol and a Convenient Assay for Superoxide Dismutase. European Journal of Biochemistry, 47, 469-474. doi.org/10.1111/j.1432-1033.1974.tb03714.x
28. American Diabetes Association, Diagnosis and classification of diabetes mellitus. Diab Care 2005;28:37-42
29. Deshmukh S, Singh VB, Chetan Kumar H, et al. Can HbA1c be a marker for cardiovascular risk in type 2 diabetes mellitus. Int J Med Res Rev. 2015;3:419–423
30. Goldberg IJ. Lipoprotein lipase and lipolysis: central roles in lipoprotein metabolism and atherogenesis. J Lipid Res. 1996;37:693–707
31. Singh G, Kumar A. Relationship among HbA1c and lipid profile in Punjabi type 2 diabetic population. J Exercise Sci Physiother. 2011;7:99–102. doi:10.18376//2011/v7i2/67614
32. Walden C, Knopp R, Wahl P, Beach K, Strandness E. Sex differences in the effect of diabetes mellitus on lipoprotein triglyceride and cholesterol concentrations. N Engl J Med. 1984; 311: 953-9.

33. Uusitupa M, Niskanen L, Siitonen O, Voutilainen E, Pyorala K. Ten year cardiovascular mortality in relation to risk factors and abnormalities in lipoprotein composition in type 2 diabetic and non-diabetic subjects. Diabetologia. 1993; 36: 1175-84
34. Odishaw, H., & Smith, W. E. Geophysical Monograph Series American Geophysical Union, 2016, 9(3), 1005–1008.https://en.wikipedia.org/wiki/American_Geophysical_Union
35. Ruiz C, Alegria A, Barbera R, Farre R, Lagrda MJ. Lipid peroxidation and antioxidantenzymes activities in patients with type I diabetes mellitus. Scand J Clin Lab Invest. 1999;59:99-105. 28. DOI: 10.1080/00365519950185823
36. 34. Ramesh Chandra Thanna, Shreya Nigosker Level of Serum ferritin and Glycated hemoglobin (HbA1C) in type 2 diabetes mellitus. International Journal of Medical and Health Research. ISSN: 2454-9142.
37. L. S. Patil, Dr. Timmanna Giraddi, Dr. Deepak Chinagi, Dr. Prasad Ugaragol and Dr. Banashankari Kolluru, 2017. "A study on relation between serum ferritin and glycatedhemoglobin in type 2 diabetes mellitus", International Journal of Current Research, 9,(08), 55849-55853.
38. Shetty JK, Prakash M, Ibrahim MS. Relationship between free iron and glycated hemoglobin in uncontrolled type 2 diabetes patients associated with complications.Ind J Clin Bio 2008;23(1):67-70
39. Kim NH et al. Serum ferritin in healthy subjects and type 2 diabetic patients. Yonsei Med J 2000;41(3):387-92.